REMARKS

Claims 1-10, 14-52, 58-60 and 65-68 are pending in this application. Claims 1-10 and 14-52 are withdrawn from consideration. Claims 11-13, 53-57 and 69-72 have been cancelled. Claims 58-60

Anticipation

The Examiner maintains the rejection of claims 58-60 and 65-68 under 35 U.S.C. 102(e) as being anticipated by *Morris* and notes that the claims supposedly read on any of thousands of combinations of epitopes of SEQ ID NO: 4, and since antibodies do not require all residues of the epitope for binding the antibody of *Morris*, such antibodies would also bind to SEQ ID NO: 4, and thus, all of the limitations of the claims have been met.

First, the *Morris* reference does not anticipate the claimed invention as it does not specifically disclose antibodies to Seq. ID No. 4. Rather, *Morris* mentions generally that antibodies can be made to the listed proteins, and provides a list of literally thousands of proteins. There is no suggestion or teaching to select the *particular* protein identified by the Examiner from that list of thousands, and then further to make an antibody to it. The *Morris* reference only generally alleges that the laundry list of protein sequences are carcinoma-associated but nowhere describes any particular utility or function of the sequence resembling Seq. ID No. 4. See paragraph [0020], for example. It is not a fair reading of *Morris* that it explicitly or implicitly teaches or discloses antibodies to that particular protein.

The *Morris* reference teaches that generating protein sequences may involve cloning the gene, and verifying its frame and amino acid sequences, or comparing it to known sequences to search for homology to provide a frame, *assuming* that the carcinoma-associated protein has homology to some protein in the database being used, as disclosed in paragraph [0085] of the reference. Thus, *Morris* admittedly does not recognize any particular utility for the disclosed sequence, and there is no reason given in *Morris* why one of skill in the art would select that peptide for further study. Yet, for this reference to anticipate, it must not only teach selection of this peptide from among thousands for further study, but then teach that such study would include making antibodies. Finally, these hypothetical antibodies would have to specifically and inevitably recognize the peptide of Seq ID No. 4, although this is far from certain given the

expected impact of the particular substitutions on the protein folding, as discussed in the previous response.

Indeed, a person of ordinary skill in the art is not taught by *Morris* to select the particular sequence located by the Examiner only by search with reference to Seq. ID No. 4, and to then prepare antibodies targeted to the *Morris* sequence. A person of ordinary skill in the art, even upon reading the *Morris* reference, would face a three-prong challenge: 1) this person would have to select a given *Morris* nucleotide sequence from thousands of nucleotide sequences, and then select and make the corresponding protein, without recognizing the purported utility of the protein sequence or having any reason or guidance provided by *Morris* for such a selection; 2) this person would then decide to generate an antibody that would target this alleged similar *Morris* protein sequence, and 3) the antibody to the *Morris* sequence would inherently have to cross-react with Seq. ID No. 4. There is no teaching or motivation in *Morris* for a person to select the targeted sequence and prepare such antibodies; there is no evidence that the antibodies would *inherently* or inevitably cross react with the protein of Seq ID No. 4. Therefore, the *Morris* reference does not anticipate the claims as recited.

Moreover, the *Morris* reference, fails to adequately enable a person of ordinary skill in the art to prepare the claimed antibody. Where anticipation of certain biotechnological inventions happens to be concerned, the Federal Circuit has already determined that a general teaching or suggestion is not sufficient for anticipation if implementing the teaching would require undue experimentation. In *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Med. Ed. and Research*, 346 F.3d 1051, 1052, for example, the Federal Circuit held that prior disclosure of a mutation associated with Alzheimer's disease together with a general teaching of a transgenic animal having the mutation would not anticipate Elan's claims to transgenic rodents having the mutation if the general disclosure of transgenic animals would require undue experimentation to reduce to practice.

In the instant case, selecting the claimed antibody from the broad genus of antibodies to any of the thousands of protein disclosed in *Morris*, particularly in the absence of any teaching as to the utility of the proteins, would require undue experimentation. As the Federal Circuit has held, "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." *Metabolite*

Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species). The Examiner's single prior art reference therefore fails to teach "each and every element" as described within the given claims for the present invention, and thus does not anticipate. *See*, *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987).

Moreover, even if *Morris* specifically disclosed antibodies to the specific protein disclosed therein, it is not certain that these proteins would inherently cross react with Seq. ID No. 4 so as to anticipate the claimed invention. The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). The Examiner has failed to meet that burden in this case.

It is certainly correct as a general statement that antibodies can bind to various sites within a disclosed amino acid sequence, and that antibodies may have similar affinity for similar proteins. It is equally true that changes in amino acid sequence, particularly significant changes as in this case, may have unpredictable effects on affect antibody binding. As stated in the

earlier response, *Morris* discloses two mismatches, a natural amino acid, a Leucine at position 925, instead of a Proline, the only natural amino acid having secondary α-amino group, as disclosed in the sequence by the applicant, and a polar amino acid, Threonine at position 936 instead of a non-polar amino acid, Methionine. These are non-conservative substitutions that would be expected to have an impact on the folding, three-dimensional structure, and electron profile of the peptide, all of which could unpredictably affect the binding of a given antibody. Thus, while antibodies to the protein of *Morris* might recognize the protein of Seq. ID No. 4, the Examiner has failed to show that this would *necessarily* be the case.

Moreover, the claims are not obvious over the *Morris* reference because there is no reason for a person of ordinary skill in the art to select the *Morris* sequence from among thousands of possible amino acid sequences disclosed, and then generate an antibody targeting that selected *Morris* sequence. A prima facie case of *obviousness* considers the *Graham* factors:
1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims in issue; 3) determining the level of ordinary skill in the pertinent art; and 4) evaluating any evidence of secondary considerations. Indeed, MPEP 2144.08 states that a finding of obviousness involves making a determination whether one of ordinary skill in the art would have been motivated to select the claimed species or subgenus. For example, a prior art genus containing only 20 compounds and a limited number of variations in the generic chemical formula inherently anticipated a claimed species within the genus because one skilled in the art would envisage each member of the genus. MPEP 2144.08, pg. 2100-156, citing *In re Petering*, 301 F.2d 676,681, 133 USPQ 275, 280 (CCPA 1962). This is not the case here. Selecting a desired protein sequence from thousands of combinations and then generating an antibody for that sequence would be "undue experimentation." Furthermore, the situation presented is not even "obvious to try," where a person of ordinary skill in the art would choose from a finite number of identified, predictable solutions with a reasonable expectation of success. Selecting from among thousands of protein sequences clearly involves a large number of possibilities and then making a second step of generating an antibody for the selected antibody, without any reason to do so, is a step not well within the skill of a person of ordinary skill in the art. Therefore, the *Morris* reference does not render the claims obvious.

As the *Morris* reference neither anticipates nor renders obvious an isolated antibody that specifically recognizes a protein as recited in the claims, the rejection under 35 U.S.C. §102(e) should be withdrawn.

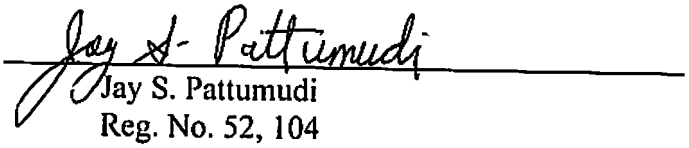
Antedating the *Morris* reference

The declaration of one of the inventors, Ruth Chiquet-Ehrismann, which is attached, shows that her invention antedates *Morris*. Specifically, the inventors reduced the claimed invention to practice prior to the filing date of *Morris*, as shown in Exhibits A-C. Exhibit A is an excerpt from a laboratory notebook describing the expression and characterization of tenascin-W in bacteria. Exhibit B is an e-mail from the inventor to an external company, RCC, confirming an order to have rabbits immunized with mouse tenascin-W expressed in *E.coli*. Exhibit C is correspondence from RCC company confirming the immunization protocol and referencing the rabbit serum generated using the disclosed Tenascin-W, which serum comprised antibodies to tenascin-W. The declaration confirms that these antibodies prepared to mouse tenascin-W will cross-react with human tenascin-W. In addition, the declaration of the other co-inventor, Arnaud Scherberich, testifies to the same affirmations relating to Exhibit A and Exhibit C. He also confirms that the antibodies prepared to mouse tenascin-W will cross-react with human tenascin-W. Accordingly, the claimed invention was actually reduced to practice prior to *Morris*. Therefore, *Morris* is antedated.

The Applicants respectfully request that the Examiner consider the arguments and the declarations and allow the pending claims. Should the Examiner have any questions or concerns, we urge the Examiner to contact Jay Pattumudi or Thomas Hoxie at the below-listed number. Please charge the requisite RCE fee to our deposit account No. 50-4255. It is believed that no other fees are required, but if this is not the case, please charge any additional fees, or credit any overpayment, to deposit account No. 50-4255.

Respectfully submitted.

Date August 6, 2009



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